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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
09/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/978,634	RABBANI ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *275,289,290 and 296-301* is/are pending in the application.

4a) Of the above claim(s) *289,290 and 298-301* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *275,296 and 297* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-3-2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on June 30, 2009.

Currently, claims 275, 289-290, and 296-301 are pending. Claims 289-290 and 298-301 have previously been withdrawn as being drawn to non-elected inventions. Accordingly, claims 275 and 296-297 are under examination on the merits in the instant case.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

Claims 275 and 296 remain rejected under 35 U.S.C. 102(b) as being anticipated by Engelhardt et al. for the reasons of record as set forth in the Office action mailed on December 30, 2008 and for the reasons stated below.

Applicant's arguments filed on June 30, 2009 have been fully considered but they are not persuasive. Applicant argues that the claims are not anticipated because Engelhardt et al. do not teach an essential element: the presence of proteins that are covalently bound to a nucleic acid. Applicant further argues that the covalent attachment is discussed in a different context in Engelhardt et al. as labeling nucleic acids with ligands. Before discussing Engelhardt et al., it is found that the meaning of "covalent bonding" or "covalent attachment" is described in the instant specification such that the covalent bonding or attachment between a protein and a nucleic acid can be made by chemical methods described in Engelhardt et al. (US 5,260,433), which is fully incorporated in the instant specification by reference. Further, the specification also states that ligands (proteins) can be attached to the nucleic acid as described in Engelhardt et al. (US 5,260,433). See pages 39-40 and 59. Note that the Engelhardt et al. (US 5,260,433) is the very prior art reference applied in the instant rejection. Hence, applicant explicitly acknowledges through the explicit disclosure in the specification that covalent attachment between protein and a polynucleotide can be made as taught and described by Engelhardt et al. (US 5,260,433), which therefore suggests that the allegedly missing essential element "the presence of proteins that are covalently bound to a nucleic acid" is logically and necessarily disclosed in the prior art of Engelhardt et al. (US 5,260,433). Hence, whether of not Engelhardt et al. disclosed the covalent attachment in a different context from what is meant or claimed by the claims is irrelevant to the patentability of the claimed subject matter because as applicant has disclosed in the specification, one skilled artisan would recognize that one can make a multimeric composition comprising a protein ligand covalently attached to a polynucleotide by using chemical methods described in the Engelhart et al. reference. Note that the claims do not recite the mechanism or manner in

which the covalent attachment is made between the protein and the polynucleotide. Hence, the chemical methods of covalent attachment between a nucleic acid and a protein described in Engelhardt et al. are sufficient to guide one skilled in the art to make the instantly claimed multimeric composition, thereby anticipating the claimed invention.

Applicant argues that the proteins disclosed in Engelhardt et al. are not ligands that bind to cell surface receptors by pointing out column 24 that the only proteins disclosed are enzymes as possible Sig moieties. Contrary to applicant's argument, the disclosure of Engelhardt et al. is not limited to Sig moieties or enzymes. As stated above, the Engelhardt et al. patent discloses that as a general principle one can make a hybrid construct comprising a protein ligand and a polynucleotide by covalently attaching the ligand and the polynucleotide. Engelhardt et al. also teach that hormone (protein) ligand binds its cognate receptor. See column 26, lines 44-49. Applicant argues that the content of column 26 shows that the ligands are referred to as small organic molecules and not proteins. It is found that the term "protein" claimed and used in the instant application embraces "an antibody, a hormone, a growth factor, a lymphokine or cytokine and a cellular matrix protein" as defined by applicant. See for example original claim 91 and pages 42 and 53 of the specification. Hence, given the broadest, reasonable interpretation in light of the applicant-defined definitions and teachings of the instant specification, the "hormone" in Engelhardt et al. is within the meaning of the "protein" as defined by applicant and as intended and claimed by applicant and thus read on the claimed "protein" (see claim 275), which is claimed to be a hormone (see claim 296). Further, Engelhardt et al. teach that example 3 pertaining to hormone receptors shows "the ligand bound to the nucleic acid reacts with a naturally occurring protein." See column 26, lines 61-64.

Applicant argues that there is no disclosure of attaching a protein ligand to an A:U double-stranded polynucleotide and that Engelhardt et al. only disclosed modified nucleotides containing the Sig moiety. First, as stated above, Engelhardt et al. disclosed the concept of "the ligand bound to the nucleic acid reacts with a naturally occurring protein." See column 26, lines 61-64. Second, with regard to the nucleic acid, Engelhardt et al. teach that it can be a double-stranded polynucleotide of DNA or RNA such as A:U polynucleotide, which can function as an interferon stimulator. In fact, Engelhardt et al. teach the advantage of using the A:U double-stranded polynucleotide because it "would be more effective and more powerful in inducing or stimulating agents for the production on interferon and related materials from cells." See column 27, lines 16-43. Third, even if the Sig moiety is included in the ligand bound to double-stranded A:U polynucleotide, there is no language in the claims that excludes the Sig moiety. Further, the disclosure of Engelhardt et al. is a comprehensive literature that is not limited to making a nucleic acid having a Sig moiety. The U.S. patent provides numerous aspects of basic principles and methods of making nucleic acid compositions, from which one can make the claimed multimeric composition because the reference provides all the elements and structural limitations necessary to synthesize the claimed composition. Accordingly, this rejection is maintained.

Claim 275 remains rejected under 35 U.S.C. 102(b) as being anticipated by Myers for the reasons of record as set forth in the Office action mailed on December 30, 2008 and for the reasons stated below.

Applicant's arguments filed on July 3, 2009 have been fully considered but they are not persuasive. Applicant argues that the structure taught in Myers is different from that of instantly

claimed invention such that the Myers monomeric units are hybridized to each other rather than to a common matrix polynucleotide. It is noted that the binding matrix claimed in the instant case does not exclude the presence of a protein as the claim recites "said binding matrix is a polynucleotide comprising sequences", wherein the "comprising" is an open-end transitional phrase and thus can include a protein. Further, Myers taught "***one or more*** selected foreign polynucleotide***s*** (nucleic acid***s*** such as DNA or RNA)" or "piece***s*** of nucleic acid" to which a ligand is chemically coupled, wherein the polynucleotides are duplex DNA. See claims 1-2 for example. Hence, Myers taught "more than one monomeric unit" comprising a protein covalently attached to a single-stranded polynucleotide, wherein more than one monomeric unit is bound to a complementary polynucleotide. As such, the teachings of Myers are sufficient to anticipate the structure of the claims. Hence, this rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 275 and 296-297 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Engelhardt et al. and Osborne et al. for the reasons of record as set forth in the Office action mailed on December 30, 2008 and for the reasons stated below.

Applicant's arguments filed on June 30, 2009 have been fully considered but they are not persuasive. Applicant argues that there is no motivation to apply the teachings of Engelhardt et al. to the method of Osborne et al. Contrary to applicant's argument, this rejection is not based on applying Engelhardt et al. to Osborne et al. Rather, the instant rejection is based on incorporating the teachings of Osborne et al. into the teachings of Engelhardt et al. such that the insulin that specifically interacts with insulin receptor is incorporated as the protein ligand that is present in

the composition of Engelhardt et al. Applicant further argues that no protein hormones are described in Engelhardt et al. and the Engelhardt et al. reference relates to SIG moieties for signal detection. Contrary to applicant's argument, as detailed above, the ligand or hormone disclosed in Engelhardt et al. is within the applicant-defined meaning of ligand or hormone. See page 4 hereinabove. Further, as stated above, the SIG moieties exemplified in Engelhardt et al. are not the only disclosure described in Engelhardt et al. as the Engelhardt et al. is a patent literature describing wide range of biological principles. Applicant further argues that the A:U polynucleotide of Engelhardt et al. is used to stimulate immune responses, which is not suitable for using insulin. However, applicant has failed to provide reasons why combining immune-stimulatory A:U polypeptide with insulin is unsuitable for using insulin. Contrary to applicant's argument, one of ordinary skill in the art wanting to provide insulin, for example to treat diabetic patients, may want to also stimulate immune responses in the diabetic patients for various reasons such as in the case when the patients need to have stimulated immune system for their specific physiological conditions. Applicant argues that Osborn does not provide motivation to obtain multimerized insulin. In response, it is noted that the *KSR* decision forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip. op at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR,* USPQ2d at 1396) (available at http://www.USPTO.gov/web/offices/dcom/bpai/prec/fd071925.pdf) Further, although Osborn does not teach multimerized insulin, it would have been apparent to one of ordinary skill in the art wanting to deliver more than one insulin unit to recognize making a composition with multiple insulin units would provide convenience as such composition would not necessitate

making multiple compositions comprising a single insulin unit. Applicant argues that even if there were motivation, one cannot arrive at the claimed composition because Engelhardt fails to teach the structure of the claimed composition. Contrary to applicant's argument, the teachings of Engelhardt et al. provide the claimed structure (see the response under 102 rejection hereinabove) and sufficient information and knowledge to make the claimed structure. Hence, this rejection is maintained.

New Rejections Necessitated by IDS Submission

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 275 is rejected under 35 U.S.C. 102(e) as being anticipated by Alul (US 5,532,130, applicant's citation).

Alul discloses an oligonucleotide of 25 nucleotides in length covalently bonded to one or more ligand molecules specific to a cell surface receptor, wherein the oligonucleotide is hybridized to its complementary oligonucleotide sequence. See claims 1, 7, 11, and 13. Note that the term polynucleotide recited in the instant claims means two or more chains of DNA or RNA. Hence, the oligonucleotide of 25 nucleotides in length of Alul necessarily comprises more

than one units of polynucleotides attached to a ligand, thereby forming a multiple units of polynucleotides covalently attached to ligands, wherein the multiple units are hybridized to a complementary polynucleotide. Accordingly, AluI discloses the structure of the claimed invention.

Conclusion

No claim is allowed.

This application contains claims 289-290 and 298-301 drawn to inventions nonelected with traverse in the reply filed on March 2, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on July 3, 2009 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635